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	Mouse VR1 capsaici	Mouse capsaicin re	Mouse DNA sequence	Mouse capsaicin re	Human VRRP-1 capsa	Human vanilloid re	Human VRRP-1 (VR2)	Human vanilloid re	Human colon cancer	Human VRRP-1 capsa	Human vanilloid re	Chicken VR1 capsai	Chicken capsaicin	Human vanilloid re	Human VRRP-1 capsa	Human vanilloid re	Human VRRP-1 (VR2)	Human vanilloid re	Rat VR1 capsaicin	re	cDNA encoding a pa	id	cDNA encoding a hu	D		vanilloid	Human vanilloid re	VR-1 codi	Human secreted pro	Human VRRP-1 (VR2)	Human vanilloid re	Human vanilloid re	Ω,	Rat partial VR-2 c

ALIGNMENTS

AAA30254 RESULT 13-NOV-1998; 28-DEC-1998; 26-FEB-1999; 19-OCT-1999; CDS VR-2; human; vanilloid receptor; nociceptor; pain signalling; hyperalgesia; musculoskeletal disorder; neuropathic pain; chromosome 17p11-12; gene therapy; ss. Human VR-2 coding sequence. (MILL-) MILLENNIUM PHARM INC 25-MAY-2000. WO200029577-A1. Homo sapiens. 05-SEP-2000 AAA30254; AAA30254 standard; 12-NOV-1999; Ļ (first entry) 98US-0108322. 98US-0114078. 99US-0258633. 99US-0421134. 99WO-US26701 Location/Qualifiers 361..2655 /product= "VR-2" /note= /*tag= a CDNA; "This region is 2809 ВP specifically claimed"

(VR2)

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Claim Page 14; 50pp; English.

This sequence represents a human vanilloid receptor-like cation channel (hVRCC) cDNA. This channel is activated by vanilloids such as capsaicin and resiniferatoxin, and is expressed in a variety of tissues, particularly in nervous tissue such as the amygdala, substantia nigra, compounds which are known to trigger cation permeability in the compounds which are known to trigger cation permeability in the compounds which are known to trigger cation permeability in the compounds which are known to trigger cation permeability in the compounds which are known to trigger cation permeability in the compounds which are known to trigger cation permeability in the compounds which are known to trigger cation permeability in the compounds which is novleved in transmission of noxious stimuli (e.g., mechanical, chemical or thermal). A recently discovered rat

compounds which are known to trigger cation permeability in the compounds which is highly expressed in dorsal root vanilloid-gated cation channel, which is highly expressed in dorsal root cannot structural homology with "store-perated" calcium channels, and is highly structural homology with "store-perated" calcium channels, and is highly selective for calcium ions. hVRCC and nucleotides encoding it can be used in prevention, diagnosis or therapy of disorders that may be associated with an excess or deficiency of hVRCC. Disorders detected or treated cusing hVRCC proteins, nucleotides or antagonists include chronic inflammation, and cannot, ulcers, autoimmune diseases, control of viscers This sequence represents a (hyRCC) CDNA. This channel and resiniferatoria inflammation, acute and chronic pain, prain viscess, control of viscera proliferation and cancer, ulcers, autoimmune diseases, control of viscera innervated by the dorsal root ganglia neurons, to mimic or antagonise innervated by the dorsal root ganglia neurons, and to inhibit graft

32 X Q

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s heat; pain; inflammation; tissue damage; nociception;
herapy; sensory neuron; immune system; analgesic; immunomo
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ng agents and in gene therapy of disorders associated with
neurons and leucocytes such as pain, autoimmune disorders
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(pos: 802..804, aa: Gly)

(pos: 955..957, aa: Lys)

(pos: 2035..2037, aa: Thr)

(pos: 2356..2358, aa: xaa)

an unspecified amino acid"
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The invention relates to 186 novel genes and their fragments (nucleic acid sequences: AAV59511-V59812; maino acid sequences AAV74731-W75026) which are useful for preventing, treating or ameliorating medical conditions e.g. by protein or gene therapy. Also, pathological conditions can be diagnosed by determining the amount of the new polynucleotides. Specific uses are described for each of the 186 polynucleotides, based on which tissues they are most highly expressed in the new polynucleotides. Specific uses are described for each of the 186 polynucleotides, based on which tissues they are most highly expressed in
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                                          The present invention relates to the human vanilloid receptor-like receptor. This receptor may be used for diagnosing or treating conditions associated with altered vanilloid receptor-like (VR-L) receptor expression. It may also be used to treat abnormal condition associated with pain. Conditions or diseases that can be diagnosed treated include viral, bacterial and fungal infections, allergic responses, mechanical injury associated with trauma, hereditory diseases, lymphoma or carcinoma, or other conditions which activate the genes of the lymphoid tissues.
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from the human cDNA clone HAFAU18 (deposited as clone ATCC 97904 and CC ATCC 209050) which encodes a secreted human protein. The gene can be used to generate fusion proteins by linking to the gene to a human CC immunoglobulin Fc portion (e.g. AAV59502) for increasing the stability of the fused protein as compared to the human protein only.

CC the invention relates to 186 novel genes and their fragments (nucleic acid sequences: AAV59511-V59812; amino acid sequences AAW74731-W75026) which are useful for preventing, treating or ameliorating medical conditions e.g. by protein or gene therapy. Also, pathological conditions can be diagnosed by determining the amount of the new polynucleotides. Specific uses are described for each of the 186 polynucleotides, based on which tissues they are most highly expressed in (see AAV59511 for described uses).
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27-JAN-1998;
26-OCT-1998;
                           The present sequence encodes a human vanilloid receptor homologue, designated VANILREP2. VANILREP2 can be used to diagnose disease or susceptibility to disease related to expression or activity of VANILREP2 polypeptides. VANILREP2 may be used to treat diseases including pain, (for example chronic, neuropathic, postoperative, rheumatoid arthritic), neuralgia, algesia, nerve injury, ischaemia.
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27-JAN-1998;
26-OCT-1998;
                                                  The present sequence encodes a human vanilloid receptor homologue VANILEEP2 polymorphic variant PVP-1. VANILEEP2 can be used to diagn disease or susceptibility to disease related to expression or active of VANILEEP2 polypeptides. VANILEEP2 may be used to treat diseases including pain, (for example chronic, neuropathic, postoperative, rheumatoid arthritic), neuralgia, algesia, nerve injury, ischaemia, neurodegeneration, stroke, incontinence, and inflammatory disorders
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2516	${\tt tgagcgctggtgcttcagggtggaggaggtgaactgggcttcatgggagcagacgctgcc}$	2457	Qy
2097	aagaagcagcgggcaggtgtgatgctgaccgttggcactaagccagatggcagcccga	03	Db
2456	aagaagcagcgggcaggtgtgatgctgaccgttggcactaagccagatggcagcccgga		Qy
2037	ctggaagctgcagaaagccatctctgtcctggagatggagaatggctattggtggtgcag	97	ф
2396	tggaagctgcagaaagccatctctgtcctggagatggagaatggctattggtggtgcag	w	Qy
1977	catgctcatcgcctcatgagcgagaccgtcaacagtgtcgccactgacagctggagcat		Db
2336	atgotcatcgccctcatgagcgagaccgtcaacagtgtcgccactgacagctggagcat	N	Qy
1917	cggcatggtgctgctgctgctggcctacgtgctgctcacctacatcctgctgctcaa	85	Db
2276	ggcatggtgctgctgctgctgctgcctacgtgctgctcacctacatcctgctgctca	Ν	Qy
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2216	otottcaaattcaccatcggcatgggcgagctggccttccaggagcagctgcacttcc	15	Qy
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1796	ttcatctggatctcgttcatagacagctactttgaaatcctcttcctgttccaggccc	7	Qy
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1736	ctgctaggggggatctacctcctcgtgggccagctgtggtacttctggcggcgccacg	6	Qy
1317	ogcccctcacctgaaagcggaagttggaaactccatgctgctgacgggccacatccttat	1258	Db
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1080	gctgtatgacctggcttctgtggacagctgtgaggagaactcagtgctggagatcattgc	1021	DЬ
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                                               This is the nucleotide sequence of cDNA coding for rat vanilloid receptor-related polypeptide 1 (VRRP-1 or VR2). The cDNA was isolated from a brain cDNA library. WRRP-1 (AAY06556) is an example of a capsalcin receptor-related polypeptide of the invention. It is not activated by capsalcin or heat, but may interact with the novel capsalcin receptor VR1 (see AAY06555). The invention provides vanilloid receptor polypeptides and polynucleotides, as well as expression vectors, host cells and transgenic animals. It also provides a method of using such receptors to identify vanilloid provides and polynucleotides.
                                                                                                                                                                                                                                                                                                                                                                                                                         New isolated capsaicin receptor polypeptide and related nucleic aci - useful for detecting vanilloid compounds, identifying modulators, and in diagnosis or treatment of e.g. pain and inflammation
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                          compounds in natural products or to screen candidate compounds that
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20-AUG-1997;

97US-0915461

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The present sequence encodes an isolated capsaicin receptor polypeptide (I). Capsaicin polypeptides are useful for identifying binding compounds which affect cellular responses. Preferably this is for identifying a compound that binds (I) and affects a cellular response associated with capsaicin biological activity (e.g. intracellular calcium flux). The polypeptides and host cells are useful for detecting a vanilloid compound (an essential structural component of capsaicin) from natural products by detecting an alteration of intracellular response associated with capsaicin receptor activity, preferably an alteration of intracellular calcium levels, and are useful for screening for compounds for use in analgesics. Capsaicin receptor polypeptides and antibodies are useful for diagnosis and treatment of human diseases and painful syndromes. The transgenic mammals can be used to screen for capsaicin receptor antagonists and agonists. Prior art methods for screening or characterising new capsaicin receptor-binding compounds relied on assays using sensory neurons in culture or in intact animals. The new
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28-DEC-1998;
26-FEB-1999;
19-OCT-1999;
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26-FEB-1999;
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27-JAN-1998;
26-OCT-1998;
designated VANILREP2, derived from EST (expressed sequence tag) sequences. VANILREP2 can be used to diagnose disease or susceptibility to disease related to expression or activity of VANILREP2 polypeptides. VANILREP2 may be used to treat diseases including pain, (for example chronic, neuropathic, postoperative rheumatoid arthritic), neuralgia, algesia, nerve injury, ischaem
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/transl_except= (pos:217..220;aa:Asp)
/note= "this codon has an apparent i nucleo
insertion which alters the reading
/transl_except= (pos:470..472;aa:Tyr)
/note= "no stop codon given"
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/product= "VANILREP2"
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                                            agatgcagcaggaggccagaggacagagcagaggatctttccaaccacatctgctggctc
                                                                                       gatggtgcctctgaggaaaactatgtgcccgtccagctcctccagtccaactgatggccc
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                                  <u>agatgcagcaggaggccagaggacagagcagaggatctttccaaccacatctgctggctc</u>
                                                                            gatggtgcctctgaggaaaactatgtgcccgtccagctcctccagtccaactgatggccc
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AAX87501
IID AAXX
XX AAX
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                                                                                                                                                                                                                                                                Query Match
Best Local Similarity
Matches 876; Conserv
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          This is the nucleotide sequence of a human vanilloid receptor-
related polypeptide 1 (VRRP-1 or VR2) partial cDNA. It codes for
the C-terminal region of a claimed WRRP-1 polypeptide (see AAY06560).
WRRP-1 is an example of a capsaicin receptor-related polypeptide of
the invention. It is not activated by capsaicin or heat, but may
interact with the novel capsaicin receptor VRI (see AAY06558). The
invention provides capsaicin receptor and capsaicin receptor
related polypeptides and polynucleotides, as well as expression
related polypeptides and polynucleotides, as well as expression
                                 1882 ctgaacctgctttactatacacgtggcttccagcacacaggcatctacagtgtccatgatc 1941
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    vectors, host cells and transgenic animals. It also provides a method of using such receptors to identify vanilloid compounds in natural products or to screen candidate compounds that modulate capsaicin receptor function for use as analgesics (vanilloid
                                                                                                                                                              1822 tgtttcctggccatcgagtggtacctgcccttgcttgtgtctgcgctggtgctgggctgg
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       analogues, therapeutic antibodies, antisense oligonucleotides, capsalcin receptor-encoding polynucleotides for gene therapy), classalcin receptor-related polypeptides and specific antibodies can also be used for the
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             New isolated capsaicin receptor polypeptide and related nucleic acid - useful for detecting vanilloid compounds, identifying modulators, and in diagnosis or treatment of e.g. pain and inflammation
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 Vanilloid receptor-related polypeptide 1; VRRP-1; VR2; capsaicin receptor; VR1; human; vanilloid; analgesic; pain; inflammation; therapy; diagnosis; ss.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           AAX87501 standard; DNA; 884 BP
                                                                                                                                                                                                                                                                                                                                                                                                                               Sequence 884 BP; 182 A; 247 C; 267 G; 181 T; 7 other;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               diagnosis and treatment of human disease and pain.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       Claim 8; Page 90-91; 120pp; English.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    WPI; 1999-469113/39
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 22-JAN-1998;
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 (REGC ) UNIV CALIFORNIA.
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          61
                                                                                                                            1 tgtttcctggccatcgagtggtacctgccctgcttgtgtctgcgctggtgctgggctgg 60
ctgaacctgctttactatacacgtggcttccagcacacaggcatctacagtgtcatgatc 120
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                                                                                                                                                                                                                                                                Conservative
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Pred. No. 9.8e-158;
5; Mismatches 2;
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2722 tggggtcccagtgaattctggtggcaaatatatattttcactaactcaaaaaa 2774 	Qу
2662 agatgcaggaggccagaggacagagcagaggatctttccaaccacatctgctggctc 2721	Qy Db
2602 gatggtgcctctgaggaaaactatgtgcccgtccagctcctccagtccaactgatggccc 2661 	Qy
2542 gcaggtgtccctcgaactctcgagaaccctgtcctggcttcccctcccaaggaggatgag 2601 	рь
2482 gaggtgaactgggcttcatgggagcagacgctgcctacgctgtgtgaggacccgtcaggg 2541 	D Qy
2422 ctgaccgttggcactaagccagatggcagcccggatgagcgctggtgcttcagggtggag 2481 	рь
2362 gtcctggagatggagaatggctattggtggtgcaggaagaagcagcgggcaggtgtgatg 2421 	Фу
2302 accgtcaacagtgtcgccactgacagctggagcatctggaagctgcagaaagccatctct 2361 	Qу
2242 goctacgtgctgctcacctacatcctgctgctcaacatgctcatcgccctcatgagcgag 2301	Фр
2182 ggcgagctggccttccaggagcagctgcacttccgcggcatggtgctgctgctgctgctgctg 2241 	Оу
2122 gcccagtacaggggtatcctggaagcctccttggagctcttcaaattcaccatcggcatg 2181 	Оу
2062 ggccccaatgccacagagtcagtgcagcccatggagggacaggaggacgagggcaacggg 2121 	Qу
2002 ggcttcgctgtagccctggtgagcctgagccaggaggcttgggcgcccgaagctcctaca 2061	Qу
1942 cagaaggtcatcctgcgggacctgctgcgcttccttctgatctacttagtcttccttttc 2001 121 caga	Ф

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